Chapter

You Have a New Super Power: Ethics of Oocyte Cryopreservation

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Abstract

This chapter will be an ethical analysis on challenging situations surrounding oocyte cryopreservation treatment in young healthy women. There has been always a complicated interaction between technology and changing societal values. This ethical discussion is not on whether or not oocyte cryopreservation in itself is ethically justifiable. Through a comprehensive literature review, this chapter discusses some ethical aspects that have emerged since oocyte cryopreservation was applied for the first time. Through a practical approach, this chapter address ethical uncertainties presenting case studies, ethical questions and terms, existing arguments in favor and against oocyte cryopreservation; and examine the individual patient's beliefs, perception and opinions.

Keywords: Egg freezing, Oocyte cryopreservation, Non-medical reason, Reproductive technology, Ethics

1. Introduction

Fertility preservation is a recent technology that provides the possibility to maintain reproductive ability to women who either face the risk of infertility for medical treatments or want to postpone childbearing for possible age-related fertility. The majority of users of Fertility Preservation technology are women who for cancer therapies receive chemo and radiotherapy that can cause infertility [1–3]. However, there are more conditions that required medical treatment can damage reproductive cells such as autoimmune diseases and myelodysplastic syndromes. Women affected by X trisomy, X-fragile, premature ovarian failure (POF) based on genetic origin as in Turner syndrome mosaicism, and syndrome, are another group that fertility preservation could help them [4]. Finally, the last group of women who can benefit from fertility preservation are those who wish to preserve and store oocytes for non-medical purposes. This procedure is called with various names such as elective egg freezing; social egg freezing, and planned oocyte cryopreservation also known as OC.

The first successful result of OC technique was a baby has born from a previously frozen oocyte in 1896, in the US [5]. Until 2012 OC has been classified as experimental by the ASRM but after a review of the scientific literature the Committee announced that the success rate of in vitro fertilization (IVF) using fresh eggs and frozen eggs are positively similar, so that they removed the experimental label from OC treatment. In addition, the existent studies about the health of babies born from frozen eggs did not prove a remarkable congenital anomalies

raise when compared with other IVF babies [5]. However, while the ESHRE, ASRM and Ethics Committee approved the use of OC for Medical reasons (mostly patients affected by cancer therapies) [5, 6]. they declined the use of OC for healthy women who wish to avoid age related fertility decline for postpone the maternity (for social reasons). In spite of not being recommended OC for non-medical reasons because of insufficient data on "safety, efficacy, ethics, emotional risks, and cost-effectiveness" the number of women seeking OC for social reason as well as the numbers of clinics offering OC technique have been increasing [7–9].

One year after removing the experimental label from OC, ASRM published an article in their website in which they explained about how healthy women can benefit from OC technique to postpone childbearing [10]. This article declared that although this new medical technique is improving, it raises "ethical issues involving evaluation of evidence, balancing benefits and harms, supporting patient autonomy, avoiding conflict of interest, and promoting advances in health care" [10].

This chapter addresses the ethical issues that arise when OC is used by women whose goal is to protect their ability to have children in the future apart from an immediate threat from gonadotoxic therapy. This ethical discussion is not on whether or not oocyte cryopreservation in itself is ethically justifiable. Through a comprehensive literature review, this chapter argues some ethical uncertainties, ethical questions and terms, existing arguments in favor and against oocyte cryopreservation; and examine the individual patient's beliefs, perception and opinions.

2. Ethical uncertainties

The OC technology improvement itself was not the only reason for women's interest to postpone childbearing. In many countries, the number of women who defer childbearing to their thirties has been rising [11]. For decades, women have been having children at older ages due to substantial lifestyle changes worldwide. By 1970, the average age of the first childbirth increased to around thirty years old, which at that time was the last chance to try for motherhood. With increasing knowledge about women's reproduction and fertility, since 1980 more women started to have children at 40–45 years old [12, 13]. Among all the reasons that affected this social change, access to education and increasing participation at workplace were the most significant. Since for women the age range (20s and 30s) in which they can peruse their education and improve their social position is also the same period of being optimal fertile (20s and early 30s) and starting to weakening at late 30s [14].

Terms such as "postponing the maternity" or "delay childbearing" are often used, which refers to the idea that the most important women's duty "motherhood" is at risk and if they do not accomplish this responsibility they are blamed to be selfish and irresponsible [15]. While studies show that, many women face conflicts in their life because the optimal moment for educational and professional improvement coincides exactly with when their reproductive system is in its best condition. Other issues such as partnership and economic situation has been also reported as other barriers on women's path for childbearing at younger age. Many women who wanted to have children find themselves in an inacceptable economic condition or not having an adequate partner [16–19]. Finally, what seems like a delay might be a consequence of the extensive and continuous overestimation of female reproductive potential with age and the capacity of reproductive treatments to recover the potential [20].

Given these societal and personal reasons for late reproduction, a biological treatment emerges because the older women are the higher risk of failure to conceive as both the quantity and quality of the oocytes decreases, while chromosomal abnormalities causing fetal abnormalities increases. Men's age also affects fertility

and offspring health, although not until men are older, age 40 or 50. For both men and women, the more time passes before they reproduce, the risk of some disorders, life circumstance, or accident may affect their fertility or abnormality in offspring.

Traditionally women, who wish to become a mother at younger ages, had the possibility to undergo IVF with donor oocytes, when they face oocyte quality problem or other diseases. Planned OC offers a further option for women in this condition, if they have previously stored their own oocytes, might help them to become mother. Compared with using donor oocytes, planned OC provides benefits such as genetically related with the off spring. Although planned OC ultimately will be ineffective in some percentage of cases, it will allow some women and couples who otherwise would have had to forego biological parenthood the chance to have genetically related children.

With this background, let us consider some of the ethical arguments in favor and against oocyte cryopreservation. A wide range of viewpoints on planned OC have been presented by researchers and commentators [21–27], while several commentators raise questions and concerns about planned OC, most conclude it should be available to women who are fully informed and wish to use it [24, 26].

2.1 Arguments supporting oocyte cryopreservation by healthy women

In 2012, the European Culture of Human Multiplication and Embryology (ESHRE) validated a plan to safeguard the richness of arranged OC [28]. The main advantage of planned OC is that it provides reproductive autonomy, by giving women greater number of reproductive options. There are several contributors to this argument. First, by giving women time to flourish in their education and careers, planned OC reduces the pressure of the 'ticking biological clock' and the pressure of having a child when the woman is not yet financially, emotionally, or situationally ready [17, 29–31]. Although all these factors are obvious benefits, recent research suggests that the lack of a partner is one of the main reasons a woman preserves her oocytes compared to other reasons [27, 32]. While oocyte freezing at a younger age gives the best chance to preserve oocyte quality, critics argue that an overreliance on genetic parenthood using this method might negatively impact and even stigmatize parents from pursuing other, more traditional options [15, 33].

The second strong argument for promoting planned OC is to give more control to women with regards to their preserved gametes compared to frozen embryos. In the case of embryos, which already has genes from the egg and the sperm, a divorce or separation could result in a partner retracting consent. This leads to additional difficulties on the clinical, emotional and legal front, which can be avoided by freezing individual gametes.

Thirdly, oocyte freezing is a more acceptable option for those who are not comfortable with preserving embryos due to moral and religious reasons [27, 34]. Indeed, some theologists trust ovarian cryopreservation and subsequent autologous transplantation later in life as morally acceptable because it does not rely on IVF for procreation [35]. Furthermore, women are allowed a possibility of having a genetically related child even if they do not have a partner when the oocytes are preserved. Hence, even though embryo cryopreservation is the more established procedure, women prefer oocyte preservation because of the independence it gives them from their partner [36].

It is to be noted that oocyte cryopreservation in this context is not performed in response to the onset of disease; rather, it is meant as protection against future infertility. The benefits of oocyte conservation by women are comparable to the cryopreservation of sperm by men, however, the costs, physical demands and the risks of the two procedures are completely different. Nevertheless, men face far less criticism when trying to preserve their future fertility compared to women [19].

A few authors note that planned OC may increase social justice by removing the obstacles that women face when planning for a family due to their shorter reproductive windows. Planned OC can minimize the burden of career and education that women face in their most fertile period and can extend their reproductive timeframe. Although this could significantly contribute to equality between men and women, this is currently not the case because of low uptake of the process in certain populations [19, 21, 28]. It is possible to postulate that women would feel and act equal to men if given the choice to extend their reproductive age. This could eventually mean women becoming mothers at 50 or 60 years of age, while currently they face biological constraints around the age of 40 [37].

Critics argue that advanced maternal age could be detrimental to children as older parents could have lesser energy to look after young children and might die before the children grow into young adults [31, 38]. However, preliminary data shows that most women actually plan on using their frozen oocytes in their 40s, and would rarely consider becoming parents in their 50s or 60s, mainly because of the higher risks to health that women face in advanced maternal age [30].

Interestingly, women who do become parents at an advanced age report that they have less pressures of establishing a career and more financial freedom, which gives them more time to focus on their family and enjoy parenthood [39]. Indeed, there is no conclusive evidence to show that younger mothers are better mothers, and more empirical data collected through longitudinal studies on children will help answer this. Nevertheless, a strong argument against older mothers is that women play important roles as grandmothers, and advanced maternal age would prevent children from enjoying social contact with their grandparents [38].

2.2 Arguments opposing oocyte cryopreservation by healthy women

A major hurdle in the advancement of routine oocyte cryopreservation is its safety [40], in addition to potential repercussions for future children and for mothers who choose pregnancy at older age. Several precautions should be taken, as there is a high level of uncertainty, with extra discretion applied when cryopreserving oocytes. There is currently not much data surrounding the harm to the health of children born from frozen oocytes, however; early reports suggest that these children do not have adverse health outcomes compared to children born without these interventions [41, 42].

Indeed, the Ethics Committee of the American Society for Reproductive Medicine lays out several arguments that planned OC is potentially safer than OC before gonadotoxic therapy in response to disease, because the patient is not already suffering from a serious disease nor are they delaying treatment due to fertility concerns [19]. Interestingly, ovarian hyperstimulation syndrome, the most common risk of OC, is actually decreased when the OC is planned because there is no embryo transfer once the stimulation cycle is finished. Additionally, it has been shown that the use of gonadotropin-releasing hormone agonist triggers can lead to a further reduction in the risk of ovarian hyperstimulation when they are used with gonadotropin releasing hormone antagonist cycles [43].

The committee hypothesizes that data on the long-term safety and efficacy of planned OC is not widely available because of the time involved in patients returning to use their cryopreserved oocytes and in the time it takes for the children derived from those oocytes to grow up. Additionally, the process of vitrification for easy cryopreservation was only recently adopted.

Another strong argument against the use of OC is the 'false hope' that the procedure might offer to women who are planning their future children [40]. Although the technique is undergoing significant advancements, live birth rates with

cryopreserved oocytes are still low and this is difficult to predict before a pregnancy progresses. This, in addition to the fact that OC does not guarantee success for a future pregnancy, poses a significant risk for waste of resources both in terms of time and money [27, 44]. The emotional wellbeing of a woman is also under threat when she relies on this technique for her reproductive goals.

In all, the committee strongly believes that a woman must make an individual choice when it comes to using planned OC after assessing the risks involved and the benefits derived from the procedure. This 'false security blanket' issue is especially relevant when planned OC is thought of as an 'insurance policy' for women who want to bear children in the future, which can pose problems when women develop an overreliance on this technique for their reproductive goals. However, the concern of overreliance assumes without prior evidence that women will dismiss other available options such as reproduction or immediate marriage, just because of cryopreserving oocytes [15].

Education and informed consent are the best ways to address patient misunderstanding of the success rates of planned oocyte cryopreservation. Towards this, physicians and other healthcare professionals involved in the process must observe restraint when describing the technique to avoid giving false hope. However, when there is a risk of overreliance on any one method of conception, it is common for patients to struggle in their decision-making process. It is important to present appropriate medical counseling to these patients and it is imperative for the healthcare provider to place trust in the patients' capability to make an informed decision when all information is duly presented. Essentially, patient choice should not be removed because of physician bias in underestimating their capabilities. More research into this topic will be crucial to address these biases.

Current research is looking to address questions about the number of oocytes, classified by age and hormone levels, that are needed to have a higher chance of a successful pregnancy using those oocytes [45–47]. It is important that this data is relayed to patients. For instance, if a woman knows that when is 38 years old she needs to store 25–30 oocytes in order to stand a chance of having one child, she is better informed and not falsely over reliant on the procedure [47–49].

Another downside of planned OC are its costs, which are usually paid out-of-pocket by women, with multiple cycles adding to the expense even more [45]. As discussed previously, OC is sometimes the only option for women who undergo social freezing, and for couples who cannot undergo embryo freezing due to ethical and/or religious beliefs. There are also countries where embryo freezing is prohibited through legislation. Even though embryo freezing is typically covered by insurance providers, this is not the case for elective oocyte freezing. This is partly fuelled by the position of the ASRM, which still does not encourage oocyte cryopreservation for personal elective reasons but promotes OC for cancer and other medical indications by removing the term 'experimental procedure' from its recommendations [50].

In most of the western world, especially in Europe and the United States, the cost of a single cycle of egg freezing is between $10 000–15 000. Understandably, the procedure has faced a lot of criticism regarding the cost-effectiveness of the technique. Indeed, the costs are not only limited to the retrieval and storage of oocytes. After the patient decides to use the frozen oocytes, IVF needs to be used to promote embryo formation. Recent research suggests that direct IVF conception at the age of 40 years is more-cost effective when compared to cryopreserving oocytes at 35 years followed by IVF at 40 years [51, 52]. In contrast, another study that developed a cost-effectiveness algorithm shows that the highest cost–benefit is obtained when the oocytes are cryopreserved when women are 37 years of age [53].

Recent findings also suggest that only 10% of women who opted for planned OC for social reasons came back to use them for a pregnancy [54]. This indicates that the associated costs are not being realized in most cases. Elective oocyte banking does not come with the financial advantages of oocyte freezing for medical purposes, which are often discounted through compassionate donations from specialized pharmacies or are supported through organizations raising funds for cancer patients. Additionally, many countries do not recognize the right of a woman to reproduce through this method and view OC as an elective procedure similar to plastic surgery for cosmetic purposes rather than a medical necessity. The high costs associated with OC and IVF and these social restrictions contribute to women missing chances to safeguard their future fertility.

Although some large companies have started offering planned OC as a health benefit [55], they are still very few to make a difference in a majority of women's lives. Planned OC is likely an option only for a small percentage of women, which would result in the benefits of education, career and life-stability available only to these privileged women. Indeed, there are concerns raised about the inequitable societal consequences of planned OC.

The committee also discusses a related issue in its opinion on OC before gonadotoxic therapy – and suggested that a person cannot be denied having an offspring because of their potentially shortened lifespan because of disease. However, this does not mean women can carry pregnancies without concerns about maternal age. Several studies show that the mother and baby are at increased risk with an increase in the age of the pregnant woman [56–58].

Moreover, children may undergo psycho-social trauma as a result of having an older mother compared to traditional reproductive options [38, 44]. Women should be made aware of these risks when they consider cryopreserving their oocytes [59].

Next, it is important to hypothesize the social implications of planned OC if it were to become mainstream. Although generally thought of as increasing women's choices and giving reproductive freedom, it could reduce their reproductive autonomy by not giving importance to the social structures surrounding female biology [33, 38, 40]. Moreover, there is a risk of social expectations shifting to pressure women into freezing their eggs if they want to have biologically or genetically related children while pursuing a successful career [34]. Taken these into account, what first appeared as a way of empowering women to take control of their reproductive choices by giving them the freedom to pursue their dreams without the constraints of a biological clock could turn into a tool that unknowingly oppresses them [33]. This future would see women having less of a choice in their reproductive journeys, and would be socially compelled to become a parent later in life because they have the choice to do so, and in the worst case, would be expected to refrain from parenthood completely [34]. Although this seems extreme, societal structures have evolved around oppressing women before and this can happen again. For planned OC to work successfully, measures need to be in place to ensure that the reproductive autonomy of women is maintained while achieving equality, without relying on "medicalization", which is a tendency to seek medical answers to social problems [28].

Therefore, as noted by several ethicists, an important question to answer is 'who should be qualified to offer these services'? [60]. The amount of time, money, expectations and emotions that social freezing patients involved in the cryopreservation of gametes go through must be taken into consideration. Achievable standards need to be in place to guide organizations offering cryopreservation and those advertising such services. Indeed, OC has been marketed to healthy women for a few years, even though there are safety and efficacy concerns surrounding it [61].

Studies from Spain and USA report that many clinics fail to sufficiently educate clients for them to make a well-informed decision [61, 62].

Another concern raised with respect to planned OS is the uncertain ownership of the gamete. Human eggs have become widely sought-after in the assisted reproduction of infertile women, which has led to a market of women selling their own eggs to egg banks for money [63]. This system could exploit young women who are looking for ways to make money.

A related concern with planned OC and ownership relates to the disposition of gametes in the case of an accidental death or when the donor succumbs to a disease. An important question that should be addressed with patients is how the oocytes should be disposed of in case the biological owner dies. Although this issue is raised with patients that are undergoing fertility preservation for medical reasons such as cancer therapy, this should also be an important topic of discussion with patients that are preserving their oocytes for reasons that are not medical.

Additionally, ownership must also be made clear in cases where donors become ill or impaired cognitively that raises concerns over assisting them in their reproductive goals. Moreover, some women may not agree to policies that govern their ability to give their cryopreserved eggs to third parties or to donate it to research and teaching. Another point of interest is that ASRM does not support the use of frozen gametes for the donor's relatives if the donor dies, even if biological owner specially requests it [46]. This is, however, possible in some countries. Details of cryopreservation such as how long the frozen eggs can be used, and who uses these eggs need to be discussed at the time of consent; this also requires specific policies adopted by clinics and legislation.

Finally, a major hurdle facing OC, especially for patients cured by cancer is the morality of a child born to a mother who has a deadly disease. This can be categorized into four major concerns: shorter lifespan of the mother, a recurrence of the cancer or other medical conditions that will be detrimental to the mother's health, the health of children born to women who froze their oocytes after starting gonadotoxic treatment, and a genetic disposition of cancer from the mother carrying over to the child. Eventually, provisions must be made for parenting and financial responsibilities in case a single woman uses her cryopreserved oocytes at an older age or after treatment for a fatal disease.

3. Individual patient's beliefs, perception and opinions

The concept of freezing eggs as a potential method of preserving fertility has been analyzed from various viewpoints and social science disciplines. The profile of patients who would use this technology and their reasoning behind using it are all being explored [64–67], As shown previously, most women who want to freeze their eggs are single and already have a decline in their fertility and the amount of eggs [67]. They choose to freeze their eggs because of a variety of reasons, important among them the physical, economical, structural, and personal factors. Indeed, it was found that women chose to freeze eggs because of the absence of conditions crucial for pursuing motherhood, and not because of the presence of any dominant reasons [68]. Interestingly, there have been investigations into fertility preservation and the attitudes surrounding it in several countries [69–74]. The majority of studies point towards an increasing acceptance of these technology which correlates with an increase in knowledge about them [70, 72].

These studies indeed provide necessary insights into the attitudes of women towards specific aspects of the freezing process especially from medical and

social viewpoints. Three major viewpoints of women regarding egg freezing is detailed below.

Owner of their life: This group of people identify women as being responsible for their own reproductive life, and is often associated with being a viewpoint that emphasizes an individual's choice without disturbances from outside factors. Although the right to reproduction is of utmost importance to these women, they are generally indifferent towards policies that intervene to facilitate being children at a younger age. This viewpoint assumes that egg freezing is a potential option for claiming their right to having a child.

Policy change requester: In this group of people, the predominant viewpoint is that assistant reproduction with technology is often unwarranted, especially for reasons that are not medical. It emphasizes on policies being enacted to ensure the wok-life balance of women. This viewpoint perceives policy chance as the only successful way of improving the conditions necessary to facilitate having a child and bringing them up.

Need for social information: This group of people need a debate on a societal scale. This point of view approves the use of egg freezing for both medical and non-medical purposes. The viewpoint encourages social debate to understand these questions in more detail and do not support the idea of a 'right' to have a child in this context. This viewpoint hence associates OC as a legitimate and responsible option to support socio-cultural changes and is not supportive of unnecessary regulatory intervention.

This final section details the challenges that assistive reproductive technologies face in the context of what is the traditional path to pursuing life and parenthood. For instance, women do not have access to infertility care or options for assistive reproductive technologies in several European countries [75].

Certainly, another important example is the utilization of parental leave. It is well established that men generally under-utilize parental leave while women take longer leaves of absence from work to care for young children. This also translates into more women with children switching to part-time work in order to facilitate the careers of men [76]. Although these balances and imbalances in family and career are acknowledged in all the viewpoints discussed above, it is perceived differently in all of them.

Viewpoint one focused on individual and autonomous choices with regards to fertility and did not care to venture into understanding policy interventions. Alternatively, viewpoint two was strongly in favor of restrictions placed on reproductive technologies with a preference for changing policies to facilitate good work-life balance. Finally, viewpoint three promoted social debate with respect to egg freezing, while disapproving regulatory interventions regarding the same. These varying viewpoints on who is responsible for their choices and how it should be regulated reflects on ideas of autonomy and maternalistic tendencies.

Indeed, the current standing of the authorities on the subject through a literature review suggests that it is important for a physician to prioritize autonomous choices compared to maternalistic tendencies [28]. However, it is important to note that viewpoints that favor these maternalistic attitudes often prevail.

Interestingly, there are several different perspectives on how egg freezing and gender equality are related. These different viewpoints suggest that freezing of eggs can be used a tool to eradicate gender inequality and the discrimination that women face. In fact, viewpoint three perceives egg freezing as a responsible choice keeping in line with changes in the socio-cultural landscape. This correlates well with the thoughts of Carroll [66], who framed this as "enacting responsible reproductive citizenship". However, despite these positive changes that egg freezing can be responsible for, it is imperative to not view it is as the solution for social injustices

to women [31]. Understandably, it is important to not restrict access to egg freezing based on these debates; however, it is imperative that legislation and employers attempt to address the real reasons behind the need for delayed childbearing for working mothers [28].

Certainly, the literature suggests that it is the diversity of viewpoints surrounding egg freezing that is responsible for controversies compared to the technology of egg freezing itself. Women who decide to freeze their eggs not only deal with all the ethical issues surrounding this technology, but also have to deal with changing opinions and viewpoints on this practice in their daily life. Some of these include being pressured to freeze their eggs to be a "responsible citizen", an unrealistic understanding of the success rates of such procedures, and the stigma they face when faced with stereotypes in their environment [15, 77].

Therefore, it is important to understand that while egg freezing certainly holds benefits for women by relieving them from the pressure of the biological clock, it could be harmful in other ways by psychologically impacting their experience based on societal expectations [78]. These points need to be considered together when discussing egg freezing. It is also crucial to understand not only the opinion of women but also that of men and other groups of people who might contribute to further controversies in the decision-making process of a woman.

4. Discussion and conclusion

Several challenges that assistive reproductive technologies face stems from certain misconceptions regarding their use and a lack of understanding the power and limitation of these technologies. Adding to these challenges are dishonest marketing campaigns overestimating the success of these procedures, a difference in success rates in different clinics and a misunderstanding of the process involved in the procedures. There is an imminent need for oversight and regulation of this technology and marketing because enthusiastic entrepreneurs target women at cocktail parties and other informal events to convince them to "freeze their eggs" before it's too late, suggesting that "smart women freeze" and the others miss out. These statements and marketing strategies are ethically and morally unacceptable, especially when women are not provided the complete picture with regards to the costs, time and risks involved and the low success rates of the procedure which is typically not covered by insurance. Information such as the number of cycles to freeze enough eggs, the cost involved in each cycle of cryopreservation, including the medications and time involved, the cost of storage of eggs per year, the age-related decrease in success rates of the procedure, the cost of the use of future eggs with intracytoplasmic injection of the sperm, the risk to the women of ovarian hyperstimulation syndrome occurring as a result of ovarian stimulation and the side effects, and more importantly the chance that there will be no baby at the end of the risky procedure should all be communicated to the patient in clear terms to facilitate them making an informed decision. These discussions should also involve the fate of the gametes in case of death, disease, disability or if the donor decides to not personally use the gametes. Patients that are already confused with the options available to them will need to be guided into the system by developing trust and by portraying transparency through standardization of care. Otherwise, there is a risk that they will be further confused by the deluge of information available and might withdraw from options available to them. Finally, there is an urgent need for a change in the curriculum when training OB/GYN residents and primary care physicians to include information about fertility decline and the options available to couples and women. To eventually promote successful reproductive decision making in patients and to

respect the rights of autonomous choices of women, it is important that OB/GYNs can provide the necessary knowledge for them to make an informed decision.

Conflict of interest

The authors declare no conflict of interest.

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